

California Cancer Commission Studies***Chapter XII****Cancer of the Oral Cavity**GEORGE S. SHARP, M.D., *Los Angeles*

ORAL cancer occurs in a wide variety of forms, and in differing degrees of malignancy. A flexible treatment program is therefore required, adaptable to each individual case. In some instances, cancer is best treated by operative methods, while in others it responds best to radium and roentgen therapy alone, and in still others both surgery and radiation are required.

Cancers in the different parts of the oral cavity are similar, one to another, in several respects. For this reason it seemed advisable to combine the discussion of etiology, precancerous lesions, and differential diagnosis for all forms of oral cancer. Clinical appearance, histopathology, treatment and prognosis, however, differ so widely that they are dealt with separately for (a) tongue, (b) floor of the mouth, (c) mucosa of the cheeks, (d) gums, (e) hard and soft palate.

Early recognition of cancer determines in a high percentage of cases whether therapy will be successful and the patient will survive. For this reason, it is necessary to investigate closely whenever a patient complains of a "vague feeling of something" in his mouth. Benign tumors, though they may seem ever so insignificant, are abnormal, and may be in the process of changing toward malignancy under the influence of irritation. (Figures 1 and 2.)

The possible presence of cancer should be suspected in all such instances, and a tissue specimen should immediately be removed for microscopic examination. The excision of a sample of the growth for biopsy neither contributes to the surface spread of oral cancer nor increases the incidence of metastases. The cost of the pathologic examination should never prove a deterrent: In case of needy patients, most pathologists, upon request of the physician, perform it without charge.

ETIOLOGY

Among the factors responsible for oral cancer, the most frequent are chronic irritation, and inflammation. They may be brought on through oral sepsis, various dental factors, and excessive use of tobacco. The dental factors include periodontal disease, advanced dental caries, injury due to jagged, broken, worn, or rough teeth, and ill-fitting dentures. Oral cancer seems, furthermore, to be related to a group of constitutional diseases, as for instance avitaminosis (especially vitamin B deficiency), hypochromic

anemia, and syphilis. A positive reaction to a Wassermann test does not mean that cancer is not present. It may well be that oral cancer never de-

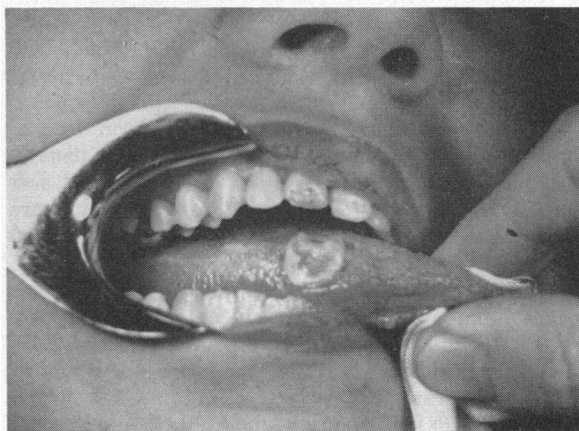


Figure 1.—*Chronic Non-Specific Ulcer.* A granular ulceration, 1.5 cm. in diameter, is seen on the right border of the tongue, midway between tip and lingual tonsil. It has a greyish tinge and is firm, but not indurated. The treatment of choice for all non-specific chronic ulcers is simple excision of the lesion for the purpose of biopsy as well as therapy.



Figure 2.—*Tuberculosis.* A superficial, granular and sloughing ulceration, 1.5 cm. in diameter, is seen on the right side of the floor of the mouth. The lesion is of soft consistency; the margin is fairly well defined, but not rolled. The patient has active pulmonary tuberculosis.

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velops from any single one of these factors, but rather from an interplay of a number of conditions, or from a specific constitutional susceptibility.

PRECANCEROUS LESIONS

The term "precancerous" implies only the possibility, not the inevitability, of malignant degeneration. In certain abnormal states, the oral mucosa is more likely to undergo cancerous change. It has to be assumed that mucous membrane which upon extraneous stimulation produces leukoplakia, keratosis, or immediately cancer, may be inherently abnormal in its tissue reactions. Therefore, the designation "precancerous" should rather be applied to such an abnormal type of mucous membrane, than to the states resulting from anomalous tissue reaction, of which leukoplakia is the most frequent. Inflammations or leukoplakia, singly or combined, were encountered in the mucous membranes of about 50 per cent of all patients with oral cancer. Leukoplakia is most commonly encountered on tongue (Figure 3) and gums, and in later stages usually becomes more diffuse, to cover the hard and soft palate. The factors responsible for leukoplakia are identical with those of cancer itself, enumerated previously.

Clinically, leukoplakia appears in the early stages as a non-palpable, faintly translucent white discoloration. Later on, localized or diffuse papillary plaques of irregular outline develop, opaque white in color, and of fine granular texture. In the late stage, which occurs only in certain cases, the epithelium piles up, forming a more or less circumscribed, thick, white covering of the organ involved. In this phase, characterized by induration, the mucous membrane becomes thick and stiff, and fissures, papillomas (Figure 4) and ulcers are encountered, which must be considered malignant until proven otherwise by biopsy. Furthermore, papillomas, fibromas, lipomas, and even small mucous cysts may become covered by leukoplakia.

DIFFERENTIAL DIAGNOSIS

Definite distinction between cancer and benign lesions is possible only on the basis of microscopic examination. A specimen, several millimeters in diameter, should immediately be removed from the edge of the growth by means of a scalpel, biting forceps, or curved specimen forceps, in such a manner that the tissue will not be crushed.

While there are certain characteristics which may tend to distinguish between benign and early malignant lesions they are so common to both that they cannot be depended upon.

Every thickening on a broad base, all small ulcers, and even a loose tooth which cannot be traced to periodontal disease, must be regarded as an indication of cancer, until proven otherwise *through biopsy*.

CANCER OF THE TONGUE

Eighty per cent of cases of cancer of the tongue occur in the male. It is more frequent along the lateral borders (50 per cent), and on the dorsum

(30 per cent), than at the tip (10 per cent), or base (10 per cent) of the tongue.

Lingual carcinoma usually starts as a minute area of overgrowth, noticeable upon digital palpation. As a rule, invasion of the submucosa and the muscularis takes place early, and produces an indurated nodule



Figure 3.—*Benign Papilloma with Superimposed Leukoplakia, Precancerous.* A benign papilloma, 1.5 cm. in diameter, and growing from a narrow base, is seen on the undersurface of the right border of the tongue. Due to irritation by the teeth, leukoplakia has developed on the surface of the papillomatous growth.

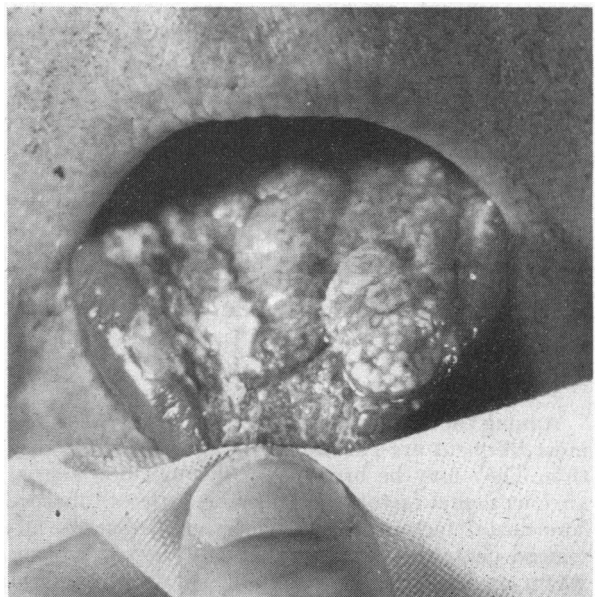


Figure 4.—*Extensive Leukoplakia with Secondary Papillomatous Growth.* The entire dorsum of the tongue is covered by leukoplakia which has caused deep, firm ridges. On the left side, a papillomatous growth has developed, which is slightly elevated, irregular, and firm, but not indurated. Repeated biopsies failed to show evidence of cancer.

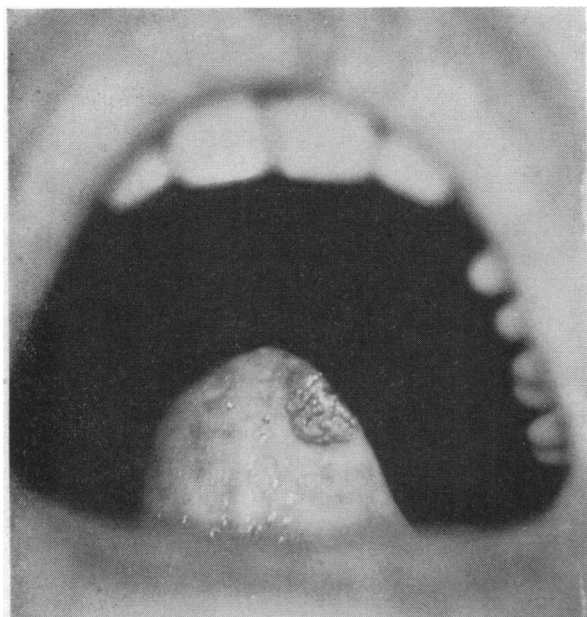


Figure 5.—*Papillary Type of Cancer, Grade I.* On the left side of the tip of the tongue, a papillary, villus-like tumor, 1.0 cm. in diameter, can be seen. The contour of the tongue has not been changed. The growth is of firm consistency, but not indurated. Apparently it has remained superficial, and no appreciable invasion of the muscularis has taken place.

on and just beneath the surface. Routine examination of the oral cavity should always include digital palpation. Any thickening, plaque, or ulcer, be it ever so small, should be considered as potentially cancerous, and immediately removed for diagnosis.

The superficial overgrowth characteristic of epidermoid carcinoma appears in one of three different forms: Papillary, nodular, or ulcerous.

A *papillary* growth suggests an early stage of the lesion. The tumor is villus-like, or ulcerated. The lesion may persist in the papillary form for months, and only moderate infiltration take place.

Nodular tumors (Figure 5), suggesting an early stage, are common on surfaces least subjected to irritation. Nodular lesions are elevated, sometimes even dome-shaped. The mucosa is smooth and has a pearly appearance. Invasion of submucosa and muscularis occurs early.

Superficial ulcers (Figures 6 and 7), either of primary origin or secondary to papillary or nodular growth appear in 80 per cent of all instances and are highly aggressive. Primary ulcers start as a small "sore spot," producing only a faint sensation of pain. Induration has to be considered as pathognomonic of cancer.

Ulcerous growths in their later stages present the appearance of a crater with indurated and rolled edges, characteristic of actively invading neoplastic tissue. (Figures 8 and 9.) Regional tenderness is invariably encountered. In far advanced cases, the sensation of pain is referred to the ear and temporal regions. Carcinomatous ulcers may at any time become secondarily infected, leading to infiltration, excavation, and metastases.



Figure 6.—*Nodular Cancer.* On the posterior third of the left border of the tongue, a triangular shaped, slightly elevated, non-ulcerated, but indurated growth, measuring 7.0 mm. in diameter, is seen. Its surface is smooth, but glistening, and there appears evidence of early invasion. This cancerous growth is due to primary injury from a sharp, jagged first molar tooth, and there is no evidence of a precancerous stage of this lesion.

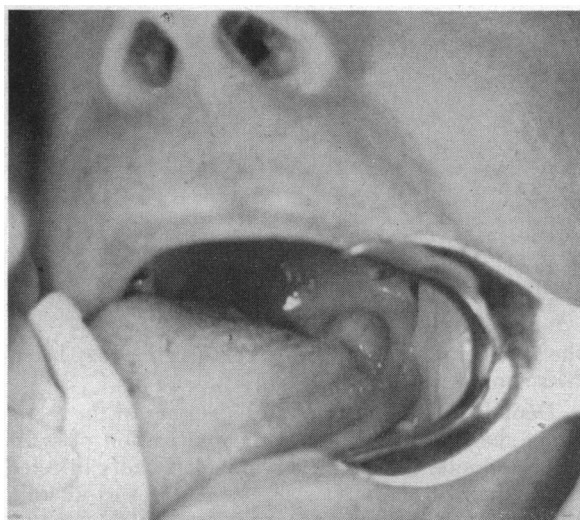


Figure 7.—*Nodular Cancer.* On the left border of the tongue, just anterior to a normal lingual tonsil, there appears a nodular, superficially ulcerated growth. The slightly dome-shaped tumor measures 1.5x1.5 cm. in diameter, while invasion in depth amounts to almost 1.0 cm.

Induration of cervical lymph nodes is always due to the presence of cancerous tissue, and indicates the existence of a primary malignant growth, almost invariably within the oral mucosa. The primary lesion is often overlooked, as it may appear as a minute, harmless-looking ulceration near the frenum, along the undersurface of the borders, or at the base of the tongue.

Histopathology: Epidermoid (squamous cell type) carcinoma is most frequently encountered (95 per cent). Other malignant lingual lesions include adenocarcinomas, and various kinds of sarcomas.

Treatment: The chances of recovery are directly related to the duration of symptoms. Treatment of primary as well as secondary lesions should therefore be started immediately.

Prophylactic oral hygiene is necessary, to check the septic condition of the mouth. While waiting for

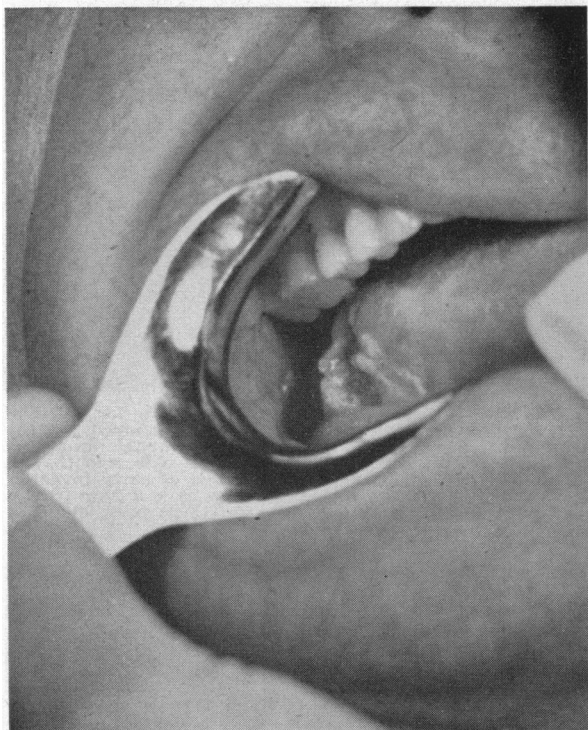


Figure 8.—*Superficial Cancer Arising on the Basis of Leukoplakia.* Along the right border of the tongue, an ulceration, 2.5x1.5 cm. in diameter is encountered. The ulcer is indurated and of irregular shape. The margin is rough and completely surrounded by moderately advanced leukoplakia. The cervical lymph nodes are not palpable, and no metastatic involvement has subsequently developed.

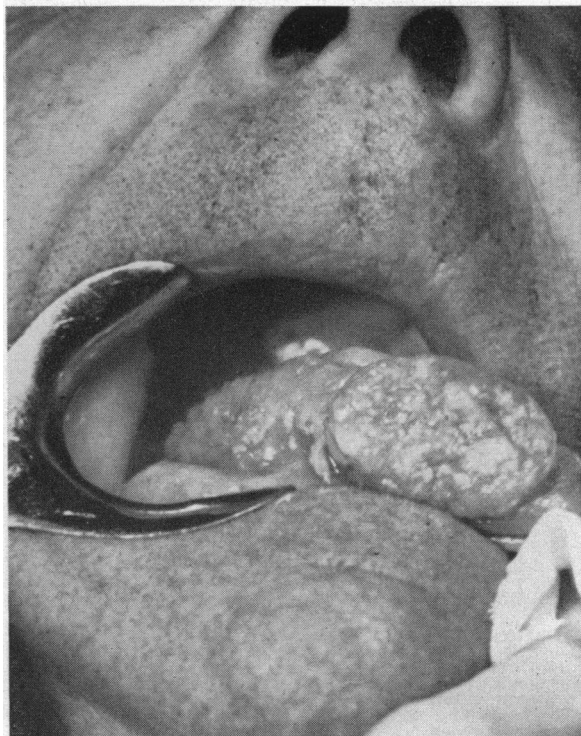


Figure 9.—*Fungating Cancer Arising on the Basis of Leukoplakia.* Along the right border of the tongue, an appears on the right border of the tongue. It is indurated, and bleeds upon slight palpation. The tumor measures 3.0x2.0 cm. in diameter, elevation above the surface of the tongue amounts to almost 1 cm., while the tongue has been infiltrated to a depth of about 1 cm. The entire lingual mucosa is covered by leukoplakia, many of the plaques are in the advanced stage, and cancer originated undoubtedly in one of these patches.

the pathologic report, treatment of the gross infection should be initiated.

Dental prophylaxis includes cleaning of the teeth, filing sharp and jagged teeth, cauterization of areas of periodontal disease, and removal of badly infected teeth. Vitamin therapy, using large doses of vitamin B complex and vitamin C, will freshen the lingual mucosa and aid the healing process.

Selection of the method for treatment of cancer of the tongue is governed by the degree of malignancy, the location and the local extent of the growth and by the presence or absence of metastases.

Treatment of the primary growth consists mainly of x-ray and radium therapy. Lesions of the tip or anterior one-third of the lateral border may be treated by wide surgical excision. Lesions at the base of the tongue are always treated with radiation. Whenever possible a peroral cone is used. It may also be necessary to supplement the x-ray therapy with either interstitial radium or radium needles. The total dosage must be calculated to destroy the cancer, yet not to inflict permanent damage to the surrounding normal cells. In 50 per cent of the cases, the primary lesion will be permanently controlled by the radiation.

In the *treatment of metastatic cervical lymph nodes*, surgical operation is the procedure of choice. Operation is feasible only under certain conditions:

The primary growth must have been unilateral, and must have been completely controlled. The involved cervical nodes must be unilateral, and on the same side as the primary growth; they must neither be fixed, nor present evidence of spread of the malignant invasion beyond the capsule. The patient's general condition must justify the risk connected with a major surgical procedure. However, cervical lymph nodes with metastatic involvement from a primary growth at the base of the tongue are always inoperable.

A radical neck dissection consists of removal of all tissues between the platysma and the deep cervical muscles, from the ramus of the mandible to clavicle and from the border of the trapezius to the midline. The sternocleidomastoid muscle and internal jugular vein must be removed.

Whenever metastatic cervical nodes prove inoperable, roentgen therapy is supplemented by implantation of interstitial radium needles or radon seeds, into the affected lymph nodes. In very advanced cases it is ill advised to employ either surgical or radium therapy, and purely palliative x-ray treatment is indicated.

Prognosis: In an unselected series of cases, the number of five-year cures amounts to 30 per cent.

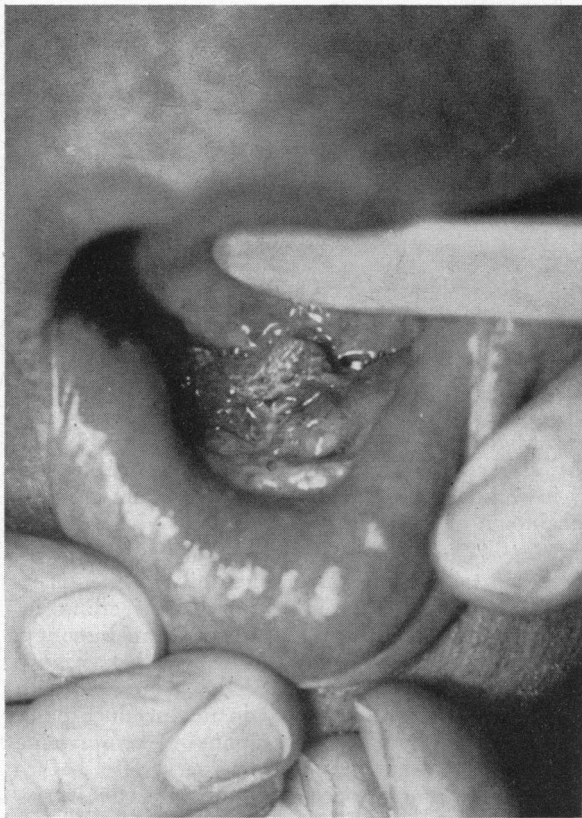


Figure 10.—*Advanced Papillary Cancer.* A papillomatous lesion, which had originated on or near the frenum, is seen on the anterior floor of the mouth. The growth has a diameter of 3.0 cm., and has completely destroyed the frenum. On both sides of the floor of the mouth, invasion has occurred; its depth, as judged by the degree of induration present amounts to 5 or 6 mm. The tongue is not infiltrated, and is still freely movable. No involvement of the cervical lymph nodes.

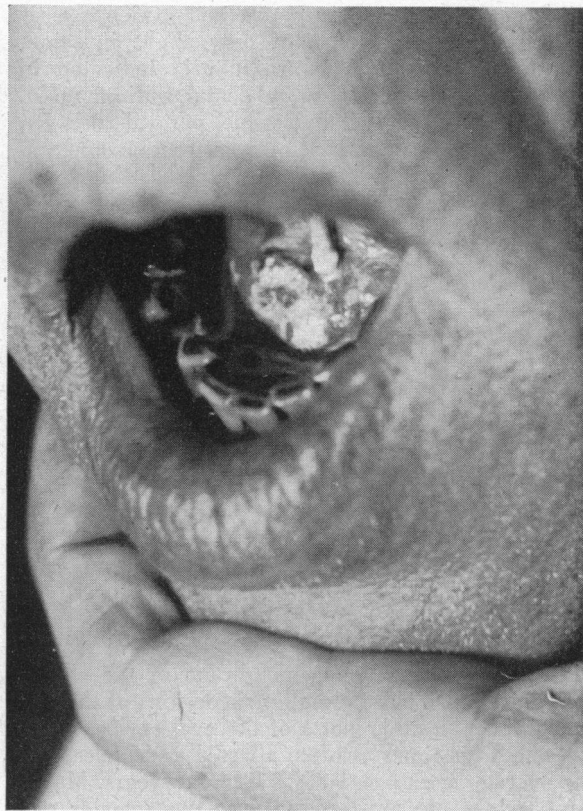


Figure 11.—*Papillary Cancer with Bulky Polypoid Overgrowth.* An oval, ulcerated growth, measuring 4.0x2.0x1.0 cm., is seen on the anterior floor of the mouth. It originated on or near the frenum, which has been destroyed in the process. The floor of the mouth has been invaded, and the growth is fixed to the mandible. The tongue has not been infiltrated. No involvement of the cervical lymph nodes.

The chances of recovery are higher when treatment is started within two months after the appearance of symptoms. The percentage of five-year "cures" is directly related to the size of the primary growth and to its location, decreasing progressively from the tip to the base of the tongue. In the presence of metastatic involvement of the cervical lymph nodes, the prognosis is much less favorable.

CANCER OF THE FLOOR OF THE MOUTH

In no other part of the oral cavity is cancer more frequently overlooked than in the floor of the mouth. Malignant tumors in this region are usually highly aggressive, and a lump in the neck often is the first symptom. When the origin of cervical metastases proves perplexing, the involvement can frequently be traced to a minute growth in the floor of the mouth.

Clinical Characteristics: Malignant lesions in the floor of the mouth often seem highly insignificant, and resemble benign ulcers which are not uncommon in this region.

Cancer assumes one of three characteristic shapes: Ulcerous, papillary, or a bulky overgrowth. Of these, the *superficial ulcer* with rolled and indurated edges

is most common. Yet, in the floor of the mouth, ulcerated tumors are less aggressive than in other parts of the oral cavity, and early invasion takes place only in the presence of constant irritation.

Papillary growths (Figure 10) are most frequently encountered at the frenum linguae, and as a rule present only slight ulceration and induration. Lesions of this type can generally be traced to malignant degeneration of benign papillomata of long standing.

Bulky growths (Figure 11) may progress to such dimensions as to displace the tongue. Such tumors are more frequent on the undersurface of the tongue than on the floor of the mouth proper.

As a rule, metastatic involvement of cervical lymph nodes occurs early; observation of the secondary growth may lead to discovery of the primary lesion. Definite diagnosis of the character of the growth, however, is possible only after microscopic examination of a tissue specimen, removed from the margin of the primary lesion.

Histopathology: Microscopically, malignant lesions in the floor of the mouth are almost always squamous cell (epidermoid) carcinoma Grade II. However, Grades III and IV are also encountered.

Treatment: The *primary growth* is preferably treated with radiation, as the mucous membrane of

the floor of the mouth responds well to this type of therapy. In the presence of only slight invasion, superficial application of radium is indicated in selected cases, using a bulky dental radium mold. Whenever the lesion is accessible, peroral roentgen therapy is indicated. If, however, tongue and anterior tonsillar pillar are also involved, this treatment has to be supplemented by interstitial radiation. In some cases surgical excision of the floor of the mouth and adjacent involved structures may be indicated.

Invasion of adjoining bone calls for surgical intervention. The operation has to include hemiglossectomy, removal of the involved parts of the floor of the mouth of the mandible, and excision of the cervical lymph nodes on the affected side.

Treatment of metastatic cervical lymph nodes proceeds generally as in the case of cancer of the tongue.

Prognosis: In an unselected series of patients with cancer of the floor of the mouth, the number of five-year "cures" amounts to about 35 per cent.

CANCER OF MUCOUS MEMBRANE OF THE CHEEKS

Cancer of the mucous membrane of the cheeks resembles more closely malignant lesions of the lips than cancer in other parts of the oral cavity. Males are about ten times as often affected as females, and the average age of patients is 62 to 65 years. Malignant lesions are most frequent in the anterior and inferior portion of the buccal mucosa.

Clinical Characteristics: Cancer of the mucous membrane of the cheeks usually assumes one of three characteristic shapes: Ulcerous, papillary, or a bulky, cauliflower-like overgrowth. *Ulcerous growths* present rolled edges and an indurated base; even in lesions which appear to be shallow, invasion has frequently extended into the muscularis.

Papillary growths are as a rule only partly ulcerated, and show little invasion in proportion to the surface area involved. The degree of malignancy is usually limited.

Bulky, cauliflower-like growths (Figure 12) are relatively rare. Outgrowth and invasion are usually of corresponding extent.

Histopathology: Malignant lesions in the buccal mucosa are almost always of the squamous cell (epidermoid) type, with differentiated cells, and formation of pearls. Malignancy of Grade II predominates.

Treatment: In lesions with a diameter of 1.0 cm. or less, surgical excision may be indicated. Growths of a larger diameter are treated with peroral roentgen ray therapy, followed by implantation of radium needles, or radon seeds.

Metastatic cervical lymph nodes are treated whenever the conditions enumerated in the section on cancer of the tongue have been fulfilled. In all other instances, only radiation is employed, combining roentgen ray therapy with implantation of radium needles, or radon seeds.

Prognosis: The incidence of serious complications

from carcinoma of the buccal mucosa is not as high as in cancer elsewhere in the oral cavity. The prognosis, however, is less favorable than in cancer of the lip, and in an unselected series of cases the number of five-year "cures" amounts to about 35 per cent. When cancer is recognized early and treatment is started without delay, the result is more favorable than in any other part of the oral cavity.

CANCER OF THE GUM

All granulations, ulcerations, and elevations on the alveolar ridges must be considered cancerous until benignity is demonstrated through microscopic examination of a tissue specimen removed from the margin of the lesion. Even in the case of alveolar giant cell tumors, treatment should never be instituted without a complete microscopic study. Invasion of tooth sockets and underlying bone, as well as infection of the primary growth, occurs early in carcinoma of the gingiva.

Clinical Characteristics: Cancer of the gum is observed in two different forms: Papillary and ulcerous. In both types, the gross appearance allows an approximate estimate of the degree of malignancy. Papillary lesions are elevated and fungating (Figure 13), but extensive surface spread is combined with little invasion. Such growths do not produce pain, but their bulk and the accompanying hemorrhage will generally cause the patient to seek relief before invasion of bone has occurred. In the early stages, the tumor forms a solid, smooth, not ulcerated mass (Figure 14), or it may be of papillary appearance, and show a certain degree of ulceration. Dentures will cause rapid spread of the primary growth, as well as early metastatic involvement.

Ulcerous lesions frequently appear as simple, mucosal ulcers. Palpation, however, will demonstrate an indurated border, which has to be considered as pathognomonic. Patients usually complain about pain and soreness interfering with mastication. Invasion is invariably extensive. On the basis of roentgenographic evidence it will be found that bone involvement in early stages is confined to the alveolar ridge, while in fully developed lesions invasion of the body of maxilla or mandible has taken place.

Histopathology: Microscopically, cancer of the gum is almost uniformly of the squamous cell (epidermoid) type. However, the two clinical forms of cancer of the gum differ also in their microscopic appearance: In the papillary type, the keratotic process may progress so far as to produce leukoplakic overgrowths, with no other evidence of malignancy than the presence of well-differentiated pearls; the invasive, ulcerous type, on the other hand, produces little keratinization or formation of pearls, but is characterized by less differentiated cellular elements.

Treatment: The primary growth is treated by surgical excision. The plan of therapy, especially the extent of the operative procedure, depends on the degree to which the bony structures have become involved. If little or no invasion has occurred, treatment consists of excision of the cancerous growth



Figure 12.—*Advanced Ulcerous Cancer.* A bulky, ulcerous tumor, measuring 3.5x3.0x2.0 cm. is seen on the anterior half of the mucosa of the right cheek. The growth has infiltrated throughout the full thickness of the cheek. Recent spread to the upper and lower lip is observed. No involvement of the cervical lymph nodes.

and of the underlying bone, combined with cauterization of a wide area. If the malignant process is no longer limited to the alveolar bone, resection of the body of the mandible, or of the maxilla, is usually required. Normal function can be adequately restored through subsequent bone graft. In the case of the mandible, it is desirable to preserve the ascending ramus, and the cosmetic result will be excellent if it is possible to re-insert the digastric muscle.

The treatment of involved cervical lymph nodes consists preferably of radical neck dissection. The indications are the same as in the case of cancer of the tongue.

Prognosis: Cancer of the gum is frequently recognized by the dentist, and the number of five-year "cures," including even cases with bone involvement, amounts to approximately 35 per cent.

CANCER OF THE HARD AND SOFT PALATE

Cancer of the palate is similar to malignant involvement of other portions of the oral mucosa. Frequently it constitutes a secondary invasion from a primary growth of the gum, the tonsil, the tongue, or within a paranasal sinus. In advanced cases, how-

ever, it may be impossible to determine at which site the malignant process started.

Clinical Characteristics: Cancerous lesions of the hard palate have the characteristic appearance of

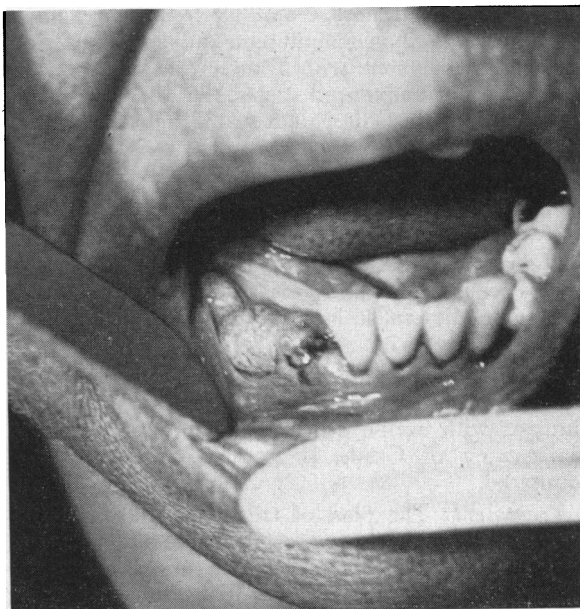


Figure 13.—*Early Cancer.* A dome-shaped, partly ulcerated growth, measuring 2.5x1.0 cm., is seen on the right lower gum. The surface is slightly nodular, and leukoplakia covers that part of the tumor which is not ulcerated. The base of the growth is surrounded by a typical rolled edge, which is indurated. The lesion is fixed to the periosteum.



Figure 14.—*Leukoplakia with Early Cancerous Change.* The entire left lower gum is covered by advanced leukoplakia. The keratotic process is more active along the external margin, where a plaque, 1.0 cm. in diameter has developed. This plaque is abnormally firm, and a slight rolled margin appears along its posterior border. Biopsy of a specimen from this area demonstrated early squamous cell epidermoid carcinoma, Grade I. No evidence of bone invasion appeared in roentgenograms, or during operation.

superficial ulcers with indurated, rolled edges, and are commonly of a diameter of 1.0 to 2.0 cm. (Figure 15). Invasion occurs late, due to the compactness of the underlying palatine bone.

On the *soft palate*, cancerous growths appear generally as bulky tumors. Papillary lesions are, however, occasionally encountered, and combine wide surface involvement with little or no invasion in depth. In more advanced stages, the disease process spreads from the soft palate to the anterior pillars of the fauces, and from there to the tonsillar fossa, the floor of the mouth, or the base of the tongue. Not uncommonly a rounded, non-ulcerative lesion is seen, due to a tumor of a minor salivary gland.

Metastatic involvement of the cervical lymph nodes occurs late, and less frequently than after primary malignant lesions in other parts of the oral cavity.

Histopathology: Microscopically, cancer of the palate appears as squamous cell (epidermoid) carcinoma, with well-differentiated cellular elements. Malignancy of Grade II is most frequently encountered.

Treatment: The plan of treatment differs in accordance with the extent of involvement, and also with the likelihood of spread of the disease process. On the *hard palate*, early growths are destroyed through cauterization. This method is not indicated in cases with invasion in depth, as a foramen into one or both nares and antra may result. In selected cases, peroral roentgen ray therapy may be substituted. Otherwise, surgical excision is the procedure of choice; the resulting gap will subsequently have to be closed by a prosthesis.

For lesions of the *soft palate*, treatment consists preferably of peroral roentgen ray therapy, alone or in combination with interstitial radiation, using radium needles, or radon seeds.

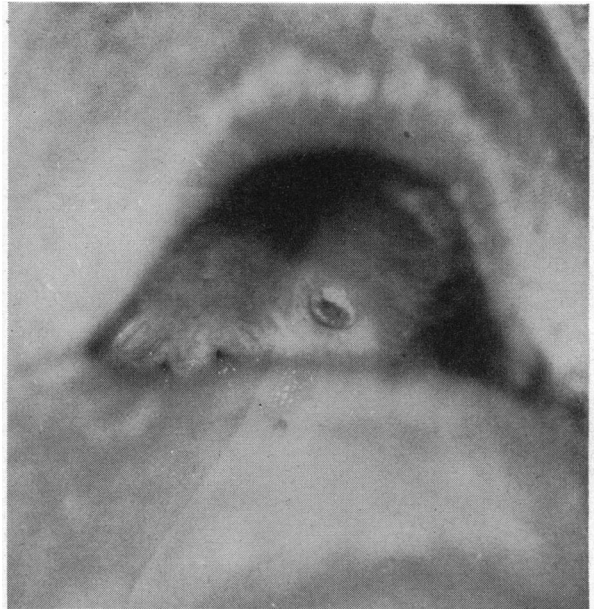


Figure 15.—*Early Cancer.* A crater-like, ulcerated growth, measuring 5.0 mm. in diameter, is seen on the left side of the hard palate. The tumor presents a granular crater with indurated, rolled edges, a characteristic sign of cancer. It is adherent to the periosteum, indicating that invasion through the submucosa has taken place.

Metastatically involved cervical lymph nodes are treated as in the case of cancer of the tongue.

Prognosis: The rate of five-year "cures" in cancer of the hard and soft palate is higher than in malignant involvement in any other portion of the oral cavity. In a series of cases, the number of five-year "cures" amounts to 40 per cent.

"Cancer of the Stomach" by H. Glenn Bell, M.D., Chapter XVIII of the *California Cancer Commission Studies*, will appear in this section of the July number of CALIFORNIA MEDICINE.

